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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/194,053	11/23/1998	MOHAMED CHOKRI	USB96AKIDM	2743

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EXAMINER
EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
1644	26

DATE MAILED: 07/29/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/194,053	Chokri et al.
Examiner	**Art Unit**
G.R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply specified above is greater than six (6) months, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *11/13/01, 1/14/02, and 5/15/02*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *44-47, 49-51, 53-55, 58, 60, and 61* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *44-47, 49-51, 53-55, 58, 60, and 61* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The request filed on 1/14/02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/194,053 is acceptable and a CPA has been established. An action on the CPA follows.

2. Applicant's election of the species IL-13 in the paper filed is acknowledged. In view of Applicant's cancellation of Claim 87, said election has been rendered moot.

Claims 44-47, 49-51, 53-55, 58, and 60-61 are pending and being acted upon.

3. In view of Applicant's Amendments and Remarks, filed 11/13/01 and 5/15/02, all previous rejections have been withdrawn, thus rendering Applicant's Remarks moot.

4. The following are new grounds for rejection.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 44-47, 49-51, 53-55, 58, and 60-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

A) Claims 44 and 55 recite "monocyte derived antigen presenting cells (MD-APCs)." MD-APCs are defined in the specification at page 6 as macrophages. Thus, the recitation of "MD-APCs having been produced by differentiating blood monocytes in vitro, in the presence of ligands enhancing the capacity of said MD-APCs for MHC-I antigen presentation relative to standard macrophages," and "MD-APCs having a greater capability of stimulating proliferation of allogenic lymphocytes relative to standard macrophages," is vague and indefinite as it comprises a recitation of a product that has enhanced properties when compared to itself, i.e., MD-APCs are macrophages.

B) Claims 45 and 58 are vague and indefinite in the recitation of "a high rate of phagocytic uptake," as a rate can only be high in comparison to another rate, and no other rate is recited.

C) In Claims 50 and 54, "cultured" would properly be "culture."

D) Claim 60 is indefinite as it depends on canceled Claim 59.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 44-47, 49-51, 53-55, 58, and 61 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the recitation of:

A) "a higher phagocytic activity (capacity) than mature dendritic cells," in Claims 44 and 55,

B) "said MD-APCs having been produced by differentiating blood monocytes in vitro, in the presence of ligands enhancing the capacity of said MD-APCs for MHC-I antigen presentation relative to standard macrophages," in Claims 44 and 55.

Applicant's amendments, filed 11/13/01 and 5/15/02, fail to assert that no new matter has been introduced into the claims. After careful review of the specification, however, specific written support for the newly introduced limitations has not been found.

9. Claims 44-47, 49-51, 53-55, 58, and 60-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention.

The instant invention is drawn to a previously undescribed type of antigen presenting cell that possesses properties of both macrophages, i.e., phagocytic capacity, and dendritic cells, i.e., superior antigen presentation. Given the unexpected nature of the cell of the instant claims, said cell must be considered highly unpredictable. As such, an enabling specification would require significant guidance and direction, and/or working examples. The specification, however, fails to adequately disclose to one of skill in the art how to make the invention of the instant claims as broadly claimed, or even that the MD-APCs of the instant claims indeed exist as a single, specific, cell type.

It is well known in the art that the culturing of monocytes with GM-CSF for a time of several days will result in the generation of dendritic cells. See for example, U.S. Patent No. 5,851,756 (Example 1). It is likely then that the culture disclosed in the instant specification comprises a mixture of dendritic cells (displaying the superior antigen presentation capacity) and macrophages (displaying the phagocytic capacity).

Regarding the guidance or direction provided by the instant specification, it is noted that the specification comprises a number of confusing disclosures. See for example, page 5 where it is disclosed that only a small percentage of the cells in culture need display particular surface antigens, used to indicate the presence (or absence) of specific cell types. For example, only 10% of the cells need express CD14 on their cell surface, and only 30% of the claimed cells in a culture need possess high phagocytic capacity. It is clear then that in this disclosure the specification is describing a mixed culture of different cell types and not the specific cell of the instant claims. Additional data also indicates a mixed cell culture, see for example Table 1, which indicates that after 7 days in culture less than half of the cultured cells comprise the claimed MD-APC. On the other hand, Table 2 indicates that after 6 days of culture >90% of the cultured cells display specific cell surface markers.

Thus, it is unclear whether the specification is describing a mixed culture or a specific cell type.

Regarding the other data that might be considered to comprise working examples in support of the MD-APCs of the instant claims, it is noted that Figure 1 discloses experimental results, yet no actual experiment is described (see last paragraph at page 14). Table 3 discloses only mixed phagocytic capacity (which could again indicate a mixed cell culture), Table 4 discloses no actual data, and Table 5 is indecipherable as it is unclear just what a percentage with a comma in the middle comprises, e.g., 97,6. Thus, it appears that the instant specification provides neither sufficient guidance nor sufficient working example to support the MD-APCs of the instant claims.

It is also noted that the claims recite specific limitations that the specification cannot support. For example, Claim 44 recites "MD-APCS which have a higher phagocytic capacity than mature dendritic cells," yet the term "mature dendritic cells" is never disclosed in the specification. The claims further recite "MD-APCs having a greater capability of stimulating proliferation of allogenic lymphocytes relative to standard macrophages," yet no demonstration of this unexpected capacity is disclosed.

Regarding the breadth of the claims, the recitation of MD-APCs differentiating "in the presence of ligands enhancing the capacity of said MD-APCs for MHC-I antigen presentation relative to standard macrophages," would indicate that numerous ligands are capable of inducing this unexpected capacity. Yet only a single combination of histamine and cimetidine is disclosed. While the specification lists a number of other chemicals assertedly capable of inducing the same unexpected and unpredictable effect, absent a showing of said capability, or at minimum an explanation of the mechanism by which said chemicals would be expected to achieve said capacity, the claim must be considered highly unpredictable. Given said unpredictability, it must be concluded that the making of the MD-APC of the instant claims would require undue experimentation.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In view of the quantity of experimentation necessary, the lack of working examples, i.e., a clear demonstration that a specific MD-APC cell type actually exists, the unpredictability of the art, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 8:00 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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Patent Examiner
Technology Center 1600
July 28, 2002